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Aldrich N.K. Lau

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EXAMINER

BERTAGNA, ANGELA MARIE

ART UNIT

PAPER NUMBER

1637

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/780,963

Applicant(s)

LAU ET AL.

Examiner

Angela Bertagna

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 March 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 and 76-84 is/are pending in the application.
- 4a) Of the above claim(s) 1-20, 25-44 and 50-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-24, 45-49, 66-74 and 76-84 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Status of the Application

1. Applicant's response filed March 15, 2007 is acknowledged. Claims 1-74 and 76-84 are currently pending. In the response, claims 21, 45, 72, and 82 were amended, and claims 75 and 85 were canceled. Claims 1-20, 25-44, and 50-65 are withdrawn from consideration as being drawn to a non-elected invention. This Office Action is made non-final due to new grounds of rejection not necessitated by Applicant's amendment (see section 3, where portions of the Ramstad reference not previously relied upon are cited; see also section 5).

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 is indefinite, because it recites the limitation "the biological sample" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 21, 24, 45, 48, 49, 66-70, 73, 76-81, and 83 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by Ramstad et al. (US 2003/0228706 A1; cited previously).

The applied reference has two inventors in common with the instant application (Harrold & Lau). Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are drawn to methods of purifying PCR and DNA sequencing products using particles comprising a core for ion-exchange and a polyelectrolyte coating.

Regarding claims 21 and 45, Ramstad teaches a method for purifying PCR reaction products or DNA sequencing reaction products, the method comprising:

(a) providing a plurality of particles, wherein each particle comprises a core for ion-exchange and a coating of polyelectrolyte (see paragraphs 70 & 71, where Ramstad teaches providing a plurality of particles; paragraph 20 teaches that the particles comprise an ion-exchange core with a coating of size-exclusion resin; paragraph 61 teaches that the size-

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exclusion resin coating is an anionic or cationic polymer (i.e. a polyelectrolyte); see also paragraphs 53-56, where Ramstad teaches that a core for ion exchange is coated with an ion exchange resin)

(b) providing a mixture of cationic ion-exchange particles and anionic ion-exchange particles, wherein the plurality of particles of step (a) are either the cationic or anionic ion-exchange particles (see paragraphs 21 & 40).

(b) contacting the PCR reaction products or DNA sequencing reaction products with the plurality of particles of step (a) to separate dsDNA fragments or dye-labeled ssDNA fragments, respectively, and purifying the PCR or sequencing reaction products (paragraph 70 teaches purification of dsDNA fragments from a PCR; paragraph 71 teaches purification of ssDNA fragments from a sequencing reaction mixture).

Regarding claim 24, Ramstad teaches that the method of claim 21 further comprises positioning a mixture comprising the plurality of particles in a column (paragraph 21).

Regarding claim 48, Ramstad teaches that the method of claim 45 further comprises removing residual dye artifacts (paragraph 71).

Regarding claim 49, Ramstad teaches that the method of claim 45 further comprises maintaining dye-labeled ssDNA fragment length (paragraph 71).

Regarding claims 66 and 76, Ramstad teaches coupling of the ion-exchange core with a PCR reaction product, such as dNTPs or salts (paragraphs 36 and 67) or a DNA sequencing reaction product, such as dye-labeled nucleotides or salts (paragraphs 36 and 69).

Regarding claims 67 and 77, Ramstad teaches that the particle is adapted to exclude dsDNA fragments greater than 100 bp (Figure 7 and paragraph 68, where a pore size excluding

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100 nt ssDNA would also inherently exclude 100 bp dsDNA) and dye-labeled ssDNA fragments greater than 45 nt (paragraph 69, where particles excluding 10 nt ssDNA would also inherently exclude 45 nt ssDNA).

Regarding claims 68 and 78, Ramstad teaches that the core comprises porous ion-exchange material (paragraphs 39, 53, and Figure 7A).

Regarding claims 69 and 79, Ramstad teaches that the ion-exchange material is surface-activated (paragraph 43).

Regarding claims 70 and 80, Ramstad teaches particles with an average pore size of 100 Angstroms (paragraph 56), thereby anticipating the instantly claimed pore size ranges of 100-2000 Angstroms and 5-1000 Angstroms, respectively.

Regarding claims 73 and 83, Ramstad teaches that the polyelectrolyte comprises polyanions and polycations (see paragraphs 53-55 and 61, where Ramstad teaches that the ion exchange core is coated with anionic or cationic ion-exchange resins and also with anionic or cationic size-exclusion resins).

Regarding claim 81, the polyelectrolyte coatings recited by Ramstad in paragraph 61 inherently possess molecular weights between 1000 Da and 6.0 MDa.

5. Claims 21, 22, 24, 45, 46, 48, 49, 66, 68, 69, 76, 78, and 79 are rejected under 35 U.S.C. 102(b) as being anticipated by Kristyanne et al. (US 6,504,021 B2; cited on IDS).

The instant claims are drawn to methods of purifying PCR and DNA sequencing products using particles comprising a core for ion exchange and a polyelectrolyte coating.

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Regarding claims 21 and 45, Kristyanne teaches a method for purifying PCR reaction products or DNA sequencing reaction products, the method comprising:

(a) providing a plurality of particles, wherein each particle comprises a core for ion-exchange and a coating of polyelectrolyte (see column 4, lines 3-27, where a charged ferrous nanoparticle core is coated with a polymeric ion-exchange resin (i.e. a polyelectrolyte); see also Example 2 at column 6, lines 10-17)

(b) providing a mixture of cationic ion-exchange particles and anionic ion-exchange particles, wherein the plurality of particles are either the cationic or anionic ion-exchange particles (column 4, lines 30-36)

(b) contacting the PCR reaction products or DNA sequencing reaction products with the plurality of particles of step (a) to separate dsDNA fragments or dye-labeled ssDNA fragments, respectively, and purifying the PCR or sequencing reaction products (Example 4, column 6, line 50 – column 7, line 12 teach purification of PCR products using the particles of step (a); column 4, lines 30-50 and column 2, lines 39-42 teach purification of sequencing reaction products using the particles of step (a)).

Regarding claims 22 and 46, Kristyanne teaches moving the PCR or sequencing reaction products through the particles using centripetal force (column 4, lines 36-40).

Regarding claim 24, Kristyanne teaches that the method of claim 21 further comprises positioning a mixture comprising the plurality of particles in a column (column 3, lines 21-25).

Regarding claim 48, Kristyanne teaches that the method of claim 45 further comprises removing residual dye artifacts (column 6, lines 40-45).

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Regarding claim 49, Kristyanne teaches that the method of claim 45 further comprises maintaining dye-labeled ssDNA fragment length (column 2, lines 49-51 and column 6, lines 40-45).

Regarding claims 66 and 76, Kristyanne teaches coupling of the ion-exchange core with a PCR reaction product, such as primers, dNTPs, or salts (column 2, lines 42-45) or a DNA sequencing reaction product, such as dye-labeled nucleotides or salts (column 2, lines 42-51).

Regarding claims 68 and 78, Kristyanne teaches that the core comprises porous ion-exchange material (column 2, lines 15-16).

Regarding claims 69 and 79, Kristyanne teaches that the ion-exchange material is surface-activated (column 4, lines 3-25, where the ion-exchange material (ionic ferrous nanoparticles) is surface-activated with ion-exchange resin).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 21-24, 45-49, 66, 68, 69, 76, 78, and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parthasarathy et al. (US 2003/0138779 A1; cited previously) in view of Kristyanne et al. (US 6,504,021 B2; cited on IDS).

The instant claims are drawn to methods of purifying PCR and DNA sequencing products using particles comprising a core for ion exchange and a polyelectrolyte coating. The claims further require providing a mixture of anionic and cationic ion-exchange particles.

Regarding claims 21 and 45, Parthasarathy teaches a method for purifying PCR reaction products or DNA sequencing reaction product, comprising:

(a) providing a plurality of particles, wherein each particle comprises a core for ion-exchange and a coating of polyelectrolyte (paragraph 15, where Parthasarathy teaches polyelectrolyte-coated anionic exchange particles)

(b) contacting the PCR reaction products or DNA sequencing reaction products with the plurality of particles of step (a) to separate and purify the dsDNA fragments or dye-labeled ssDNA fragments, respectively (see paragraphs 11, 14, and 15; see also paragraphs 53-56, which teach purification of PCR products using the coated anion exchange particles and paragraphs 59-60, which teach purification of sequencing reaction products using the coated particles).

Regarding claims 22 and 46, Parthasarathy teaches that the contacting comprises moving the PCR reaction products or the DNA sequencing reaction products through the particles using centripetal force (paragraph 74).

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Regarding claims 23 and 47, Parthasarathy teaches that the plurality of particles comprises a first volume and that the PCR or DNA sequencing reaction products comprise a second volume, wherein the first volume is greater than or equal to the second volume (Example 1 on page 11 and Example 10 on page 15 teach the use of particles in the form of membranes for purification of the reaction products. Here, five to ten microliters of sequencing reaction products or PCR reaction products were added to the membrane). Since the volume of the added nucleic acid solutions (5-10 microliters) is much smaller than the volume of the membrane, Parthasarathy teaches the limitations of claims 23 and 47.

Regarding claim 24, Parthasarathy teaches that the method of claim 21 further comprises positioning a mixture comprising the plurality of particles in a column (paragraph 32).

Regarding claim 48, Parthasarathy teaches that the method of claim 45 further comprises removing residual dye artifacts (paragraphs 11, 59, and 60).

Regarding claim 49, Parthasarathy teaches that the method of claim 45 further comprises maintaining dye-labeled ssDNA fragment length (paragraphs 59-61).

Regarding claims 66 and 76, Parthasarathy teaches coupling of the ion-exchange core with a PCR reaction product, such as dNTPs or primers (paragraphs 119-120) or a DNA sequencing reaction product, such as dye-labeled nucleotides or salts (paragraph 52).

Regarding claims 68 and 78, Parthasarathy teaches that the core comprises porous ion-exchange material (paragraph 71).

Regarding claims 69 and 79, Parthasarathy teaches that the ion-exchange material is surface-activated (paragraph 15, where coating of the ion-exchange material with polyelectrolyte results in a surface-activated particle; see also paragraphs 34-37).

Parthasarathy does not teach providing a mixture of anionic and cationic ion-exchange particles, as required by claims 21 and 45.

Regarding claims 21 and 45, Kristyanne teaches providing a mixture of cation exchange particles and anion exchange particles for purification of nucleic acids. Kristyanne teaches that treatment of a nucleic acid sample to be purified with a cation exchange resin simultaneously with or followed by an anion exchange resin results in a rapid, simple, and readily automated purification method (see column 1, line 64 – column 2, line 10 and column 2, lines 19-30).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to further include a cation exchange resin in the purification method taught by Parthasarathy. As noted above, Kristyanne taught that purification of nucleic acids, such as PCR or DNA sequencing products, was faster, cheaper, simpler, and more readily automated when a cation exchange resin was used in combination with an anion exchange resin (column 1, line 64 – column 2, line 10). An ordinary practitioner of the purification method taught by Parthasarathy would have been motivated by these teachings of Kristyanne to additionally include a cation exchange resin in order to improve the speed, simplicity, and automation capability of the method while reducing costs. Since the methods taught by Parthasarathy and Kristyanne were both directed to ion-exchange purification of PCR or DNA sequencing reaction products, an ordinary practitioner would have had a reasonable expectation of success in applying the teachings of Kristyanne to the method taught by Parthasarathy. Thus, the method of claims 21-24, 45-49, 66, 68, 69, 76, 78, and 79 is prima facie obvious over Parthasarathy in view of Kristyanne.

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8. Claims 67, 70-72, 77, and 80-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parthasarathy et al. (US 2003/0138779 A1; cited previously) in view of Kristyanne et al. (US 6,504,021 B2; cited on IDS) and further in view of Padhye et al. (US 5,658,548; cited previously).

The instant claims are drawn to the PCR and DNA sequencing product purification methods of claims 21, 68, 76, and 78, further comprising the use of a resin that excludes dsDNA fragments greater than 100 bp or ssDNA fragments greater than 45 nt. These claims also define the range of suitable pore sizes for the ion exchange material (100-2000 Angstroms, 1000 Angstroms, 5-1000 Angstroms, and 50 Angstroms) and suitable molecular weights for the polyelectrolyte coating (1.0 MDa – 3.0 MDa, 1.7 MDa – 2.4 MDa, 1000 Da – 6.0 MDa, 2.4 MDa – 4.9 MDa).

The combined teachings of Parthasarathy and Kristyanne result in the method of claims 21, 68, 76, and 78, as discussed above.

Regarding claims 71 and 81, Parthasarathy teaches that the polyelectrolyte material has a molecular weight of 2.0 MDa (paragraph 44, where the PSSA polyelectrolyte inherently has a molecular weight of approximately 2.0 MDa).

Regarding claims 67, 70, 72, 77, 80, and 82, Parthasarathy does not teach a specific pore size for the ion-exchange material.

Padhye teaches a method for isolating nucleic acids with lengths greater than about 50 bases using compositions comprising silica (see abstract). Padhye teaches application of the method to purification of PCR products from primer-dimers (Example 7, column 17, lines 31-

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61), single-stranded DNA (Example 5, column 15-16), or RNA (Examples 8 & 9, column 17-19).

Regarding claims 67, 70, 72, 77, 80, and 82, Padhye teaches that the pore size of the silica suspension used in the purification method is 30-300 Angstroms and specifically teaches use of a suspension with a pore size of 60 Angstroms (column 4, lines 23-35; see also column 10, lines 43-56). This pore size inherently excludes dsDNA fragments greater than 100 bp and ssDNA greater than 45 nt.

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize an ion exchange material in the method resulting from the combined teachings of Parthasarathy and Kristyanne with a pore size of 30-300 Angstroms. As discussed above, Padhye taught an ion exchange-based method of nucleic acid purification and specifically taught that pore sizes of 30-300 Angstroms were suitable for purification of nucleic acids longer than 50 bases (such as PCR products, ssDNA, or RNA) (see abstract and Examples 7-9, cited above). An ordinary practitioner would have been motivated by these teachings of Padhye to use an ion exchange material with such a pore size in the method resulting from the combined teachings of Parthasarathy and Kristyanne in order to ensure that the target molecules (PCR products or ssDNA) were efficiently purified by the polyelectrolyte-coated ion exchange material. In other words, an ordinary artisan would have been motivated to use the small pore size suggested by Padhye in the method resulting from the combined teachings of Parthasarathy and Kristyanne in order to obtain a more highly purified sample. Since Padhye expressly taught the use of silica resins with a pore sizes of 60, 100, or 250 Angstroms for purification of nucleic acids greater than 50 bases (column 10, lines 50-60), an ordinary practitioner would have

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expected a reasonable level of success in using ion exchange resins with similar pore sizes in the method resulting from the combined teachings of Parthasarathy and Kristyanne. Therefore, one of ordinary skill in the art, interested in increasing the purity of the sample obtained by the method resulting from the combined teachings of Parthasarathy and Kristyanne, would have been motivated to utilize a pore size of 30-300 Angstroms, as suggested by Padhye, thus resulting in the instantly claimed methods.

9. Claims 73, 74, 83, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parthasarathy et al. (US 2003/0138779 A1; cited previously) in view of Kristyanne et al. (US 6,504,021 B2; cited on IDS) and further in view of Breadmore et al. (WO 03/104774 A1; cited previously).

The instant claims are drawn to the PCR and DNA sequencing product purification methods of claims 21 and 45, further wherein the polyelectrolyte coating comprises polyanions and polycations added in alternating layers.

The combined teachings of Parthasarathy and Kristyanne result in the method of claims 21 and 45, as discussed above.

Kristyanne does not teach that the polyelectrolyte coating is comprised of alternating layers of polyanions and polycations.

Breadmore teaches a method of nucleic acid purification using silica-based extraction procedures (see pages 1-2 for a general description).

Regarding claims 73, 74, 83, and 84, Breadmore teaches increasing the yield of the purification method by modifying the silica surface with polyelectrolytes. Specifically,

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Breadmore teaches that the stability of the adsorbed polyelectrolyte layer can be improved by using multiple layers. Breadmore further teaches coating the silica particles with a cationic polymer followed by a second coating with an anionic polymer and repeating this process to form a multilayer (see page 13).

It would have been prima facie obvious for one of ordinary skill in the art to coat the ion-exchange particles taught by Parthasarathy with multiple alternating layers of polycations and polyanions since Breadmore taught that such treatment improved the stability of the adsorbed polyelectrolyte layer (see page 13, cited above). Breadmore also taught that such modifications of silica-based resins improved purification yields (see page 13), thereby providing additional motivation for an ordinary practitioner to coat the ion exchange-adapted silica particles taught by Parthasarathy with multiple alternating layers of polycations and polyanions. Since the resins taught by Breadmore were used for purification of nucleic acids, including PCR and DNA sequencing reaction products (page 2, lines 1-4), an ordinary practitioner would have expected a reasonable level of success in using ion exchange-adapted silica particles coated with multiple alternating layers of polyelectrolytes in the method taught by Parthasarathy. Therefore, an ordinary practitioner of the method resulting from the combined teachings of Parthasarathy and Kristyanne, interested in increasing purification yields and resin stability, would have been motivated to use multiple alternating layers of polyanions and polycations as suggested by Breadmore, thus resulting in the instantly claimed methods.

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10. Claims 23 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kristyanne et al. (US 6,504,021 B2).

The instant claims are drawn to the method of claims 21 and 45, respectively, wherein the plurality of particles comprises a first volume, the PCR or sequencing reaction products comprise a second volume, and the first volume is larger than the second volume.

Kristyanne teaches the method of claims 21 and 45, as discussed above.

Regarding claims 23 and 47, Kristyanne teaches that the amount of resin (particles) used in the purification method is linked to the required incubation time, and that this amount can be determined empirically by the user (column 4, lines 61-67). Kristyanne further teaches that increasing the resin volume has the advantage of decreasing the required incubation time (column 4, lines 62-64).

It would have been prima facie obvious for one of ordinary skill in the art at the time of invention to utilize a volume of resin (particles) greater than the volume of PCR or sequencing reaction products when practicing the method taught by Kristyanne. As noted above, Kristyanne taught that the resin volumes were results-effective variables that could be optimized by the ordinary practitioner (column 4, lines 61-67). Since Kristyanne further taught that increasing the resin volume decreased the required incubation time (column 4, lines 62-64), an ordinary practitioner would have been motivated to increase the resin volume in order to reduce the purification time. Moreover, as noted in MPEP 2144.05, "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235

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(CCPA 1955).” Routine optimization is not inventive, and no evidence has been presented to suggest that the selection of the claimed volumes was other than routine, or that the results should be considered unexpected compared to the closest prior art. Therefore, in the absence of secondary considerations, the claimed methods are *prima facie* obvious over the prior art of Kristyanne.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claim 45 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8 and 21 of copending Application No. 11/057,936 in view of Kristyanne et al. (US 6,504,021 B2; cited on IDS).

Claims 8 and 21 of the '936 application recite a method for DNA sequencing comprising contacting sequencing reaction products with particles comprising an ion exchange core and a polyelectrolyte coating, isolating the particles, and sequencing the purified sequencing products. The claims of the '936 application do not recite providing a mixture of cationic and anionic ion exchange particles as required by the instant claim 45. However, providing such a mixture of ion exchange particles would have been obvious in view of the teachings of Kristyanne. As discussed in greater detail above, Kristyanne taught that combining a cationic and anionic exchange step resulted in a faster, simpler, cheaper, and more readily automated purification method (column 1, line 60 – column 2, line 10). Therefore, an ordinary practitioner of the method recited in claims 8 and 21 of the '936 application would have been motivated to additionally include a mixture of anionic and cationic exchange resins with the coated ion exchange particle in order to obtain the advantages taught by Kristyanne. Thus, the instant claim 45 is prima facie obvious over claims 8 and 21 of the '936 application in view of Kristyanne.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claim 45 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12 and 15 of copending Application No. 11/355,872 in view of Kristyanne et al. (US 6,504,021 B2; cited on IDS).

Claims 12 and 15 of the '872 application recite a method for DNA sequencing comprising contacting sequencing reaction products with particles comprising an ion exchange core and a polyelectrolyte coating, isolating the particles, and sequencing the purified sequencing

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products. The claims of the '872 application do not recite providing a mixture of cationic and anionic ion exchange particles as required by the instant claim 45. However, providing such a mixture of ion exchange particles would have been obvious in view of the teachings of Kristyanne. As discussed in greater detail above, Kristyanne taught that combining a cationic and anionic exchange step resulted in a faster, simpler, cheaper, and more readily automated purification method (column 1, line 60 – column 2, line 10). Therefore, an ordinary practitioner of the method recited in claims 12 and 15 of the '872 application would have been motivated to additionally include a mixture of anionic and cationic exchange resins with the coated ion exchange particle in order to obtain the advantages taught by Kristyanne. Thus, the instant claim 45 is prima facie obvious over claims 12 and 15 of the '872 application in view of Kristyanne.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

14. Applicant's arguments, see page 20, filed March 15, 2007, with respect to the rejection of claims 21-24, 45-49, and 66-85 under 35 U.S.C. 112, 2nd paragraph, have been fully considered and are persuasive. Applicant's amendments overcome the rejections, and therefore, they have been withdrawn.

Regarding the rejection of claims 21, 24, 45, 48, 49, 66-70, 73, 75-81, 83, and 85 under 35 U.S.C. 102(a) and 102(e) as being anticipated by Ramstad (US 2003/0228706 A1), Applicant's arguments filed March 15, 2007 have been fully considered but they are not persuasive. Applicant argues that Ramstad does not teach all of the elements of independent

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claims 21 and 45, specifically the polyelectrolyte coating (see page 20). This argument was not found persuasive, because as discussed above, Ramstad teaches a polyelectrolyte coating (see paragraph 61, where Ramstad teaches that the polymeric size-exclusion resin coated on the ion-exchange core particle can be anionic or cationic; see also paragraphs 53-56, where Ramstad teaches that a core for ion exchange is coated with an ion exchange resin). Furthermore, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a polyelectrolyte that is polymerized before coating the ion-exchange core) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant's arguments, see page 20, filed March 15, 2007, with respect to the rejection of claims 21-24, 45-49, 66, 68, 69, 76, 78, and 79 under 35 U.S.C. 102(a) and 102(e) as being anticipated by Parthasarathy have been fully considered and are persuasive. Parthasarathy does not teach all of the elements of independent claims 21 and 45 as amended, and therefore, the rejection under § 102 has been withdrawn.

Regarding the rejection of claims 67, 70-72, 77, and 80-82 under 35 U.S.C. 103(a), Applicant's arguments have been considered but are moot in view of the new ground(s) of rejection.

Regarding the rejection of claims 73, 74, 83, and 84 under 35 U.S.C. 103(a), Applicant's arguments have been considered but are moot in view of the new grounds of rejection. Some of Applicant's arguments remain pertinent to the new rejection (see page 23), but these arguments

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were not persuasive. In response to applicant's argument that there is no suggestion to combine the references (see page 23), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine the references is found in the teachings cited above. As discussed above, an ordinary practitioner of the method resulting from the combined teachings of Parthasarathy and Kristyanne would have been motivated to coat the ion-exchange material with alternating layers of polyanions and polycations, because Breadmore taught that this coating increased the stability of the polyelectrolyte coating (see above). Since Applicant's arguments were not persuasive, the rejection has been maintained.

Regarding the provisional double patenting rejections citing co-pending applications 11/057,936, 11/355,372, and 11/232,036, Applicant states that a response is not required at present since the rejections are provisional (see page 23). As noted in MPEP 804, "The 'provisional' double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that 'provisional' double patenting rejection is the only rejection remaining in at least one of the applications." Since the provisional double patenting rejections are not the only rejections remaining in the instant application, the rejections are maintained as appropriate.

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Conclusion

No claims are currently allowable.

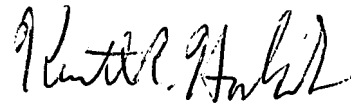
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Angela Bertagna whose telephone number is 571-272-8291. The examiner can normally be reached on M-F, 7:30 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Angela Bertagna
Art Unit 1637
May 22, 2007

amb



KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

5/24/07